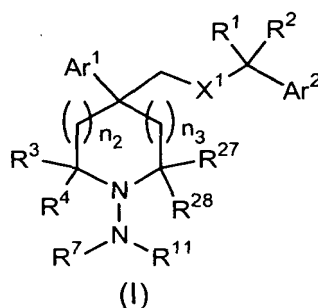


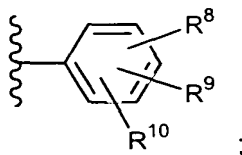
5 **What is claimed is:**

1. A compound having the formula (I):



or a pharmaceutically acceptable salt or solvate thereof, wherein

- 10 Ar^1 and Ar^2 are each independently selected from the group consisting of $(R^{19})_{n7}$ -heteroaryl- and



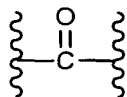
X^1 is selected from the group consisting of -O-, -S-, -SO-, -SO₂-, -NR¹²-, -N(COR¹²)- and -N(SO₂R¹⁵)-;

- 15 R^1 , R^3 and R^5 are each independently selected from the group consisting of H and C₁-C₆ alkyl;

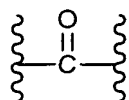
- R^2 , R^4 and R^6 are each independently selected from the group consisting of H, -CONR¹³R¹⁴ and -(CH₂)_{n1}-G; wherein G is selected from the group consisting of H, -CF₃, -CHF₂, -CH₂F, -OH, -O-(C₁-C₆)alkyl, -SO₂R¹³, -O-(C₃-C₈ cycloalkyl), -NR¹³R¹⁴,
20 -SO₂NR¹³R¹⁴, -NR¹³SO₂R¹⁵, -NR¹³COR¹², -NR¹²(CONR¹³R¹⁴), -CONR¹³R¹⁴, -COOR¹² and C₃-C₈ cycloalkyl; or

R^1 and R^2 , taken together with the carbon to which they are attached, form a C₃-C₆ cycloalkyl ring; or

R^1 and R^2 , taken together with the carbon to which they are attached, form a

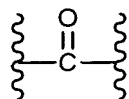


5 group, provided that X1 is -O- or -NR¹² when said



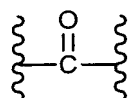
is formed; or

R³ and R⁴, taken together with the carbon to which they are attached, form a



10 group; or

R⁵ and R⁶, taken together with the carbon to which they are attached, form a



group;

15 R⁷ and R¹¹ are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, (R¹⁶)_{n7}-aryl-, (R¹⁹)_{n7}-heteroaryl-, -COOR²⁹, -CONR²¹R²², -CON(R²¹)(CH₂)_n-G¹, -S(O)_{n5}(CH₂)_n-G¹, -S(O)_{n5}R¹³, -CO(CH₂)_n-G¹ and -(CH₂)_{n1}-G¹; wherein

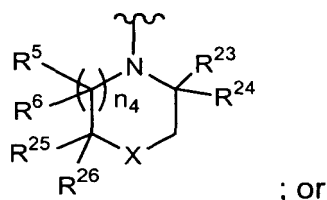
n is 0-4, and

20 G¹ is selected from the group consisting of H, -OH, (C₁-C₆)alkyl, -O-(C₁-C₆ alkyl), -S(O)_{n5}R¹³, -O-(C₃-C₈ cycloalkyl), -NR¹³R¹⁴, -SO₂NR¹³R¹⁴, -NR¹³SO₂R¹⁵, -NR¹³COR¹², -NR¹²(CONR¹³R¹⁴), -OC(=O)R¹², -CONR¹³R¹⁴, -COOR¹², C₃-C₈ cycloalkyl, -CF₃, (R¹⁶)_{n7}-aryl-O-, (R¹⁶)_{n7}-aryl-, (R¹⁹)_{n7}-heteroaryl-, (R¹⁹)_{n7}-heterocycloalkyl- and alkenyl, and

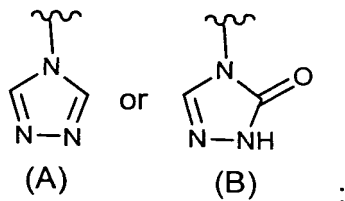
25 provided that, when n is 0, then G¹ is selected from the group consisting of H, (C₁-C₆)alkyl, alkenyl, -CONR¹³R¹⁴, -COOR¹², C₃-C₈ cycloalkyl, -CF₃, (R¹⁶)_{n7}-aryl-, (R¹⁹)_{n7}-heteroaryl-, and (R¹⁹)_{n7}-heterocycloalkyl-; and

30 provided that, when n₁ is 1, then G¹ is selected from the group consisting of H, (C₁-C₆)alkyl, alkenyl, -S(O)_{n5}R¹³, -SO₂NR¹³R¹⁴,

- 5 -CONR¹³R¹⁴, -COOR¹², C₃-C₈ cycloalkyl, -CF₃, (R¹⁶)_{n7}-aryl-,
 (R¹⁹)_{n7}-heteroaryl- wherein said heteroaryl ring is bound by a ring carbon
 to the -(CH₂)_{n1}- group, and (R¹⁹)_{n7}-heterocycloalkyl- wherein said
 heterocycloalkyl ring is bound by a ring carbon to the -(CH₂)_{n1}- group; or
 R⁷ and R¹¹, taken together with the nitrogen to which they are attached, form a
 10 5-7 membered heterocycloalkyl ring of the following formula:



R⁷ and R¹¹, taken together with the nitrogen to which they are attached, form a
 5-membered ring having the formula (A) or (B):



- 15 X is selected from the group consisting of -NR²⁰-, -N(CONR¹³R¹⁴)-,
 -N(CO₂R¹³)-, -N(SO₂R¹⁵)-, -N(COR¹²)-, -N(SO₂NHR¹³)-, -O-, -S-, -SO-, -SO₂-, -CF₂-,
 -CH₂-, and -C(R¹²)F-;
- R⁸, R⁹ and R¹⁰ are each independently selected from the group consisting of H,
 C₁-C₆ alkyl, C₃-C₈ cycloalkyl, -OR¹², halogen, -CN, -NO₂, -CF₃, -CHF₂, -CH₂F, -OCF₃,
 20 -OCHF₂, -OCH₂F, -COOR¹², -CONR²¹R²², -NR²¹COR¹², -NR²¹CO₂R¹⁵,
 -NR²¹CONR²¹R²², -NR²¹SO₂R¹⁵, -NR²¹R²², -SO₂NR²¹R²², -S(O)_{n5}R¹⁵, (R¹⁶)_{n7}-aryl- and
 (R¹⁹)_{n7}-heteroaryl-;
- R¹² is selected from the group consisting of H, C₁-C₆ alkyl and C₃-C₈ cycloalkyl;
 R¹³ and R¹⁴ are each independently selected from the group consisting of H,
 25 C₁-C₆ alkyl, C₂-C₃ alkyl-O-CH₃, C₃-C₈ cycloalkyl, (R¹⁹)_{n7}-aryl(CH₂)_{n6}- and
 (R¹⁹)_{n7}-heteroaryl-(CH₂)_{n6}-; or

5 R^{13} and R^{14} , taken together with the nitrogen to which they are attached, form a 4-7 membered ring containing from 0-3 additional heteroatoms selected from the group consisting of -O-, -S- and -NR¹²-;

R^{15} is C₁-C₆ alkyl, C₃-C₈ cycloalkyl or -CF₃;

10 R^{16} is 1 to 3 substituents each independently selected from the group consisting of C₁-C₆ alkyl, C₃-C₈ cycloalkyl, C₁-C₆ alkoxy, halogen and -CF₃;

R^{19} is 1 to 3 substituents each independently selected from the group consisting of C₁-C₆ alkyl, C₃-C₈ cycloalkyl, -OH, halogen, -CN, -NO₂, -C(O)CF₃, -CF₃, -CHF₂, -CH₂F, -OCF₃, -OCHF₂, -OCH₂F, -O-(C₁-C₆ alkyl), -O-(C₃-C₈ cycloalkyl), -COOR¹², -CONR²¹R²², -NR²¹R²², -NR²¹COR¹², -NR²¹CO₂R¹², -NR²¹CONR²¹R²²,
15 -NR²¹SO₂R¹⁵ and -S(O)_{n5}R¹⁵;

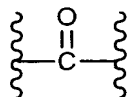
R^{20} is H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, -(CH₂)_{n6}-heterocycloalkyl, (R¹⁹)_{n7}-aryl(CH₂)_{n6}- or (R¹⁹)_{n7}-heteroaryl-(CH₂)_{n6}-;

R^{21} and R^{22} are each independently selected from the group consisting of H, C₁-C₆ alkyl, C₃-C₈ cycloalkyl and benzyl; or

20 R^{21} and R^{22} , taken together with the nitrogen to which they are attached, form a 4-7 membered heteroaryl ring containing from 0-3 additional heteroatoms selected from the group consisting of -O-, -S- and -NR¹²-;

R^{23} and R^{24} are each independently selected from the group consisting of H, C₁-C₆ alkyl and -CONR¹³R¹⁴; or

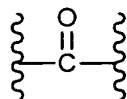
25 R^{23} and R^{24} , taken together with the carbon atom to which they are attached, form a



group;

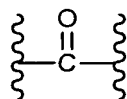
30 R^{25} , R^{26} , R^{27} and R^{28} are each independently selected from the group consisting of H and C₁-C₆ alkyl; or

R^{25} and R^{26} , taken together with the carbon atom to which they are attached, form a



group; or

R^{27} and R^{28} , taken together with the carbon atom to which they are attached, form a



group;

R^{29} is selected from the group consisting of C_1 - C_6 alkyl and C_3 - C_8 cycloalkyl;

n_1 is 1-4;

n_2 and n_3 are each independently 0-3, provided that a sum of n_2 and n_3 is 0-4;

n_4 is 0-2;

n_5 is 0-2;

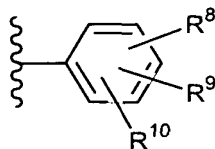
n_6 is 0-3; and

n_7 is 0-3; and

provided that, when n_4 is 0, and R^{25} and R^{26} are each H, then X is not -O-, -NR²⁰- or -S-.

2. The compound of Claim 1 wherein X^1 is -O-.

3. The compound of Claim 1 wherein Ar^1 and Ar^2 are each independently



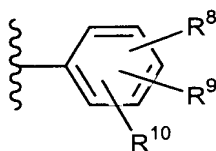
4. The compound of Claim 3 wherein R^8 , R^9 and R^{10} are each

independently selected from the group consisting of H, -CH₃, halogen and -CF₃.

5. The compound of Claim 1 wherein

X^1 is -O-; and

Ar^1 and Ar^2 are each independently

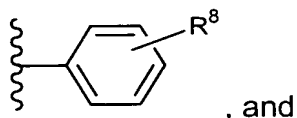


wherein R^8 , R^9 and R^{10} are each independently selected from the group consisting of

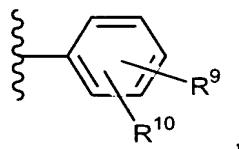
H, -CH₃, halogen and -CF₃.

6. The compound of Claim 1 wherein

Ar^1 is



Ar^2 is



wherein,

R^8 is selected from the group consisting of H and F, and

R^9 and R^{10} are each independently selected from the group consisting of H, -CH₃, F, Cl and -CF₃.

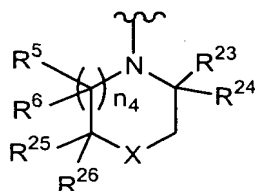
7. The compound of Claim 6 wherein

X^1 is -O-; and

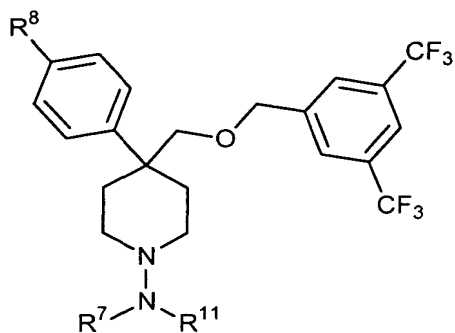
R^3 , R^4 , R^{27} and R^{28} are each H.

8. The compound of Claim 6 wherein R^5 and R^6 are H.

- 5 9. The compound of Claim 7 wherein R^7 and R^{11} , taken together with the nitrogen to which they are attached, form a 5-7 membered ring having the following formula:

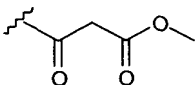
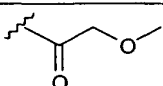
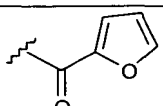
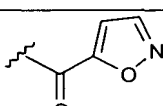
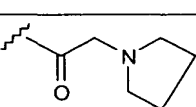
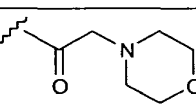
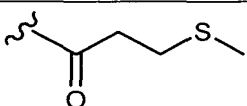
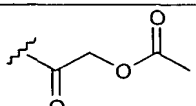
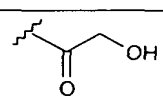
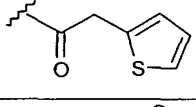
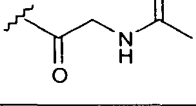
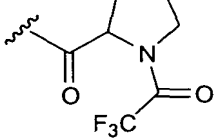


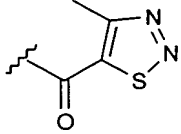
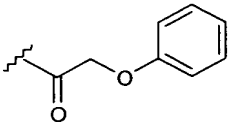


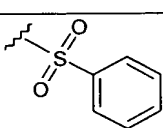
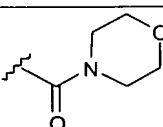
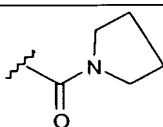
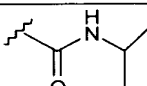
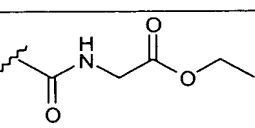
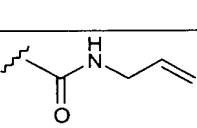
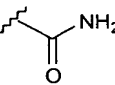
- 10 10. The compound of Claim 1 having the formula

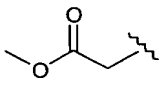
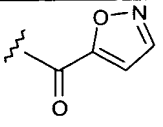
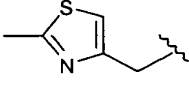
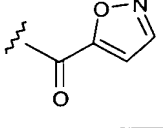
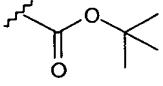
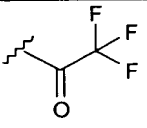
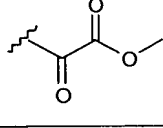
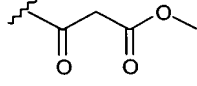
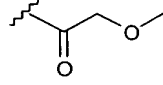
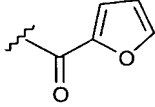
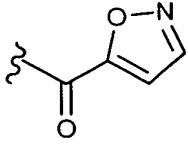
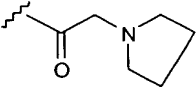
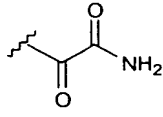


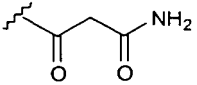
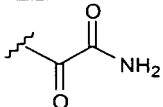
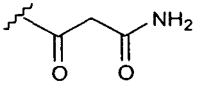
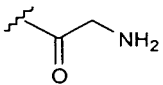
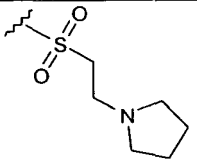
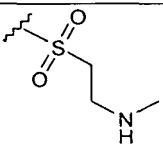
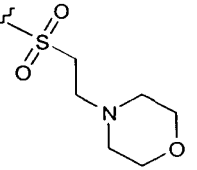
wherein R^7 , R^8 and R^{11} are selected from the group consisting of:

R^8	R^7	R^{11}
H	H	H
H	H	
H	H	
H	H	
H	H	

H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	

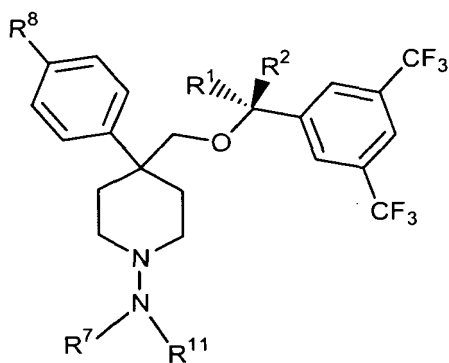
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	
H	H	

H		
H		
F	H	
F	H	H
F	H	
F	H	
F	H	
F	H	
F	H	
F	H	
F	H	
H	H	

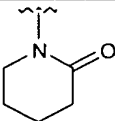
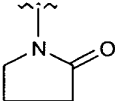
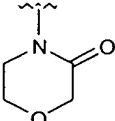
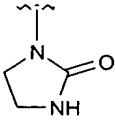
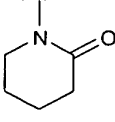
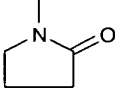
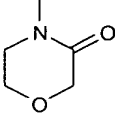
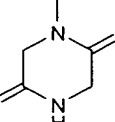
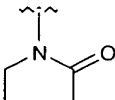
H	H	
F	H	
F	H	
H	H	
H	H	
H	H	
H	H	

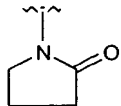
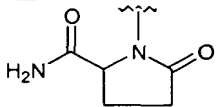
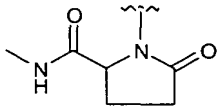
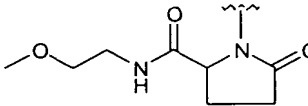
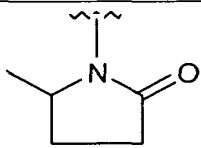
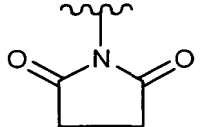
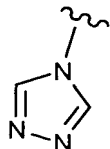
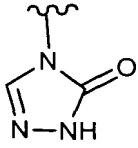
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11. The compound of Claim 1 having the formula:



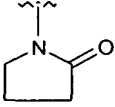
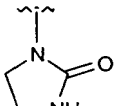
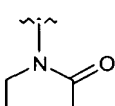
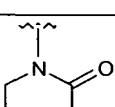
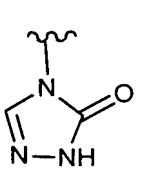
wherein R^1 , R^2 , R^7 , R^8 and R^{11} are selected from the group consisting of:

R^8	R^1	R^2	$-NR^7R^{11}$
H	H	H	
H	H	H	
H	H	H	
H	H	H	
F	H	H	
F	H	H	
F	H	H	
H	H	H	
H	H	CH ₃	

H	H	CH ₂ OH	
H	H	H	
H	H	H	
H	H	H	
H	H	H	
H	H	H	
H	H	H	
H	H	H	

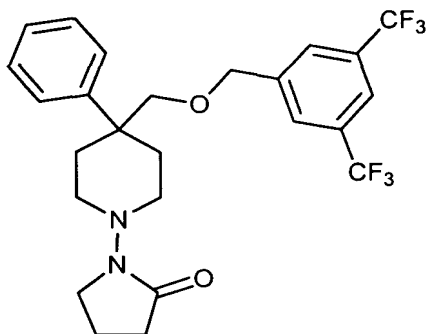
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12. The compound of Claim 11 or the pharmaceutically acceptable salt or solvate thereof, wherein R¹, R², R⁷, R⁸ and R¹¹ are selected from the group consisting of

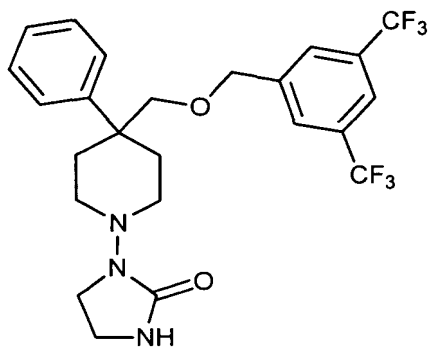
R^8	R^1	R^2	$-NR^7R^{11}$
H	H	H	
H	H	H	
H	H	CH ₃	
H	H	CH ₂ OH	
H	H	H	

5

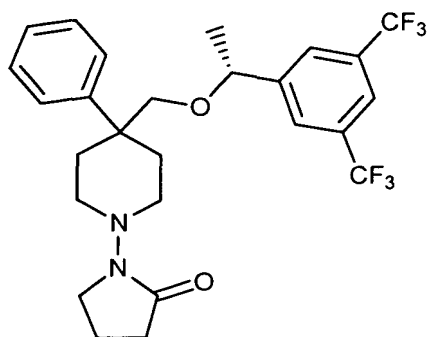
13. The compound of Claim 12 having the formula:



- 5 14. The compound of Claim 12 having the formula:

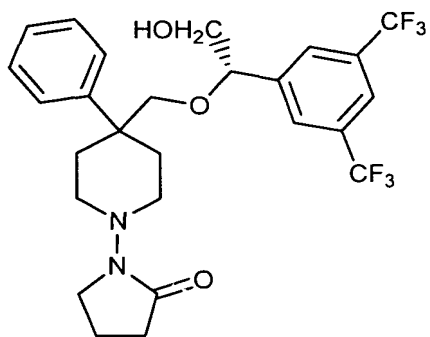


15. The compound of Claim 12 having the formula:

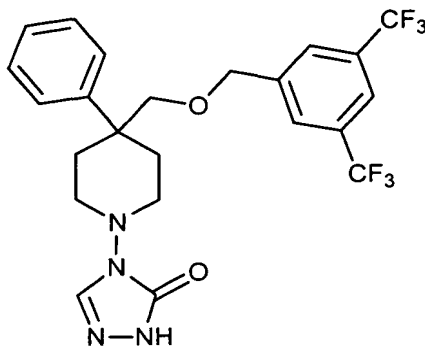


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16. The compound of Claim 12 having the formula:



17. The compound of Claim 12 having the formula:



18. A pharmaceutical composition comprising at least one compound of Claim 1, and a pharmaceutically acceptable carrier.

19. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, at least one serotonin reuptake inhibitor, and at least one compound of Claim 1.

20. A method for treating a physiological disorder, symptom or disease in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1, wherein said physiological disorder, symptom or disease is selected from the group consisting of: respiratory diseases, inflammatory diseases, skin disorders, ophthalmological disorders, central nervous system conditions, addictions, epilepsy, nociception, psychosis, schizophrenia, Alzheimer's disease, AIDs related dementia, Towne's disease, stress related disorders, obsessive/compulsive disorders, eating disorders, sleep disorders, mania, premenstrual syndrome, gastrointestinal disorders, atherosclerosis, fibrosing disorders, obesity, Type II diabetes, pain related disorders, bladder and genitourinary disorders, and nausea.

21. A method for treating a physiological disorder, symptom or disease in a patient in need of such treatment, comprising administering to said patient an effective

5 amount of at least one compound of Claim 1, wherein said physiological disorder,
symptom or disease is selected from the group consisting of: a respiratory disease,
depression, anxiety, phobia, bipolar disorder, alcohol dependence, psychoactive
substance abuse, nociception, psychosis, schizophrenia, stress related disorder,
obsessive/compulsive disorder, bulimia, anorexia nervosa, binge eating, sleep
10 disorder, mania, premenstrual syndrome, gastrointestinal disorder, obesity, headache,
neuropathic pain, post-operative pain, chronic pain syndrome, bladder disorder,
genitourinary disorder, cough, emesis and nausea.

22. A method for treating a physiological disorder, symptom or disease in a
15 patient in need of such treatment, comprising administering to said patient an effective
amount of at least one compound of Claim 1, and an effective amount of at least one
active ingredient selected from the group consisting of: other NK₁ receptor
antagonists, selective serotonin reuptake inhibitors, dopamine receptor agonists,
serotonin 5-HT₃ receptor antagonists, serotonin 5-HT_{2c} receptor agonists, nociceptin
20 receptor agonists, glucocorticoids and inhibitors of multidrug resistance protein 5,
wherein said physiological disorder, symptom or disease is selected from the group
consisting of: a respiratory disease, depression, anxiety, phobia, bipolar disorder,
alcohol dependence, psychoactive substance abuse, nociception, psychosis,
schizophrenia, stress related disorder, obsessive/compulsive disorder, bulimia,
25 anorexia nervosa, binge eating, sleep disorder, mania, premenstrual syndrome,
gastrointestinal disorder, obesity, headache, neuropathic pain, post-operative pain,
chronic pain syndrome, bladder disorder, genitourinary disorder, cough, emesis and
nausea.

30 23. A method of treating emesis and/or nausea in a patient in need of such
treatment comprising administering to said patient an effective amount of at least one
compound having the formula (I) in combination with an effective amount of at least
one serotonin 5-HT₃ receptor antagonist and/or at least one glucocorticoid.

5 24. The method of Claim 23 wherein said serotonin 5-HT₃ receptor antagonist is ondansetron and said glucocorticoid is dexamethasone.

25. The method of Claim 21, wherein the physiological disorder, symptom or disease is emesis, depression, anxiety or cough.

10 26. The method of Claim 25 wherein the physiological disorder, symptom or disease is depression or anxiety.

15 27. The method of Claim 26, further comprising administering to the patient an effective amount of at least one anti-depressant agent and/or at least one anti-anxiety agent.

20 28. The method of Claim 25 wherein depression is being treated and said method further comprises administering to the patient an effective amount of at least one selective serotonin reuptake inhibitor.

25 29. A method for antagonizing an effect of a Substance P at a neurokinin-1 receptor site or for blocking at least one neurokinin-1 receptor, in a patient in need of such treatment, comprising administering to said patient an effective amount of at least one compound of Claim 1.

30 30. A kit comprising, in separate containers in a single package, pharmaceutical compositions for use in combination to treat an NK₁ receptor mediated disease, wherein one container comprises a pharmaceutical composition comprising an effective amount of a compound of Claim 1 in a pharmaceutically acceptable carrier, and wherein, a separate container comprises a pharmaceutical composition comprising another therapeutic agent in a pharmaceutically acceptable carrier, said therapeutic agent being selected from the group consisting of: SSRIs, other types of NK₁ receptor antagonists, prostanoids, H₁ receptor antagonists, α -

5 adrenergic receptor agonists, dopamine receptor agonists, melanocortin receptor agonists, endothelin receptor antagonists, endothelin converting enzyme inhibitors, angiotensin II receptor antagonists, angiotensin converting enzyme inhibitors, neutral metalloendopeptidase inhibitors, ET_A antagonists, renin inhibitors, serotonin 5-HT₃ receptor antagonists, serotonin 5-HT_{2c} receptor agonists, nociceptin receptor
10 agonists, glucocorticoids, rho kinase inhibitors, potassium channel modulators and inhibitors of multi-drug resistance protein 5.

31. A kit comprising, in separate containers in a single package, pharmaceutical compositions for use in combination to treat depression and/or
15 anxiety, wherein one container comprises a pharmaceutical composition comprising an effective amount of a compound of Claim 1 in a pharmaceutically acceptable carrier, and wherein, a separate container comprises a pharmaceutical composition comprising an antidepressant agent in a pharmaceutically acceptable carrier, and/or wherein a separate container comprises a pharmaceutical composition comprising an
20 antianxiety agent in a pharmaceutically acceptable carrier.

32. A kit comprising, in separate containers in a single package, pharmaceutical compositions for use in combination to treat an NK₁ receptor mediated disease, wherein one container comprises a pharmaceutical composition
25 comprising an effective amount of a compound of Claim 1 in a pharmaceutically acceptable carrier, and wherein, a separate container comprises a pharmaceutical composition comprising an SSRI in a pharmaceutically acceptable carrier.

33. A kit comprising, in separate containers in a single package, pharmaceutical compositions for use in combination to treat depression and/or
30 anxiety, wherein one container comprises a pharmaceutical composition comprising an effective amount of a compound of Claim 1 in a pharmaceutically acceptable carrier, and wherein, a separate container comprises a pharmaceutical composition comprising an SSRI in a pharmaceutically acceptable carrier.

5

34. A kit comprising, in separate containers in a single package, pharmaceutical compositions for use in combination to treat emesis and/or nausea, wherein one container comprises a pharmaceutical composition comprising an effective amount of a compound of Claim 1 in a pharmaceutically acceptable carrier, and wherein, a separate container comprises a pharmaceutical composition comprising a serotonin 5-HT₃ receptor antagonist in a pharmaceutically acceptable carrier, and/or wherein a separate container comprises a pharmaceutical composition comprising a glucocorticoid in a pharmaceutically acceptable carrier.

10

15

35. A kit comprising, in separate containers in a single package, pharmaceutical compositions for use in combination to treat emesis and/or nausea, wherein one container comprises a pharmaceutical composition comprising an effective amount of a compound of Claim 1 in a pharmaceutically acceptable carrier, and wherein, a separate container comprises ondansetron, and/or wherein a separate container comprises dexamethasone.

20